

Endocrine System Biochemistry -Lec(1)

Recap :

- (1) Synthesis of hormones \rightarrow **Glands** .
- (2) Secreted then carried to their target sites of action by \rightarrow **Blood** .
- (3) Present at **very low levels** (low concentrations -micrograms) in the circulatory system .
- (4) Act specifically via receptors located on / in target tissue .

Requirements of intracellular communication :

- (1) Ligand \rightarrow signaling molecule
 - (2) Receptor protein \rightarrow can be **extracellular or intracellular** (or **transmembrane receptor like IR**)
- \rightarrow The **4 basic types of communication** :
- (1) Direct contact
 - (2) Paracrine signaling
 - (3) Endocrine signaling
 - (4) Synaptic signaling

Comparison	Nervous Sys	Endocrine Sys
Signals	Electrical impulses (APs)	Chemical impulses (Hormones)
Transmission	neurons	blood
Sped of transmission	fast	slow
Duration of effect	Short-lived	Long-lived
Control	CNS	Endocrine glands
Chemical coordinators	Very few ,called :NTs	Many different types ,called :Hormones <each one affecting diff ,specific tissue)
Target	Localized (cells connected to neuron)	Tend to affect more than one target organ .
Resp nature	Can be voluntary or involuntary	Always involuntary

(1) Direct contact \rightarrow molecules on the surface of one cell are recognized **by receptors on the adjacent cell**

(2) Paracrine signaling \rightarrow signal released from a cell has an **effect on neighboring cells** (NO , Histamine , PGs)

(3) Endocrine signaling \rightarrow hormones released from a cell **affect other cells throughout the body** (Estrogen , Thyroxine , GH , Epi).

(4) Synaptic signaling \rightarrow nerve cells release the signal (NTs) which **binds to receptors on nearby cells** .

Enzymes	Hormones
Proteinaceous in nature except for ribozymes	May be proteinaceous , amine or steroids
Secreted and act on the same place	Secretion and activation take place in diff locations
Control all biochemical rxns of the cell	Only some biochemical rxns are controlled by hormones
Play a central role in metabolism	Have a regulatory role in metabolic activities
Substrate specific	Specific to the target cell,tissue,system
Not consumed , reusable	Used up ,and degenerated after the rxn

The 4 1ry arenas of hormone action :

- (1) **Reproduction** .
- (2) **Growth&development** .
- (3) Maintenance of **internal environment** .
- (4) Energy production , utilization and storage .

★ Class'n of hormones based on their chemical structure :

Class	Examples
Peptides or protein hormones	TRH \rightarrow Tripeptide \rightarrow (Glu-His-Pro) \rightarrow Smallest peptide hormone . Insulin \rightarrow 51 aa GH \rightarrow 191aa PRL \rightarrow 198 aa Pituitary gonadotropins \rightarrow FSH ,LH (large glycoproteins w/ α and β subunits) . ACTH , Calcitonin , Glucagon , vasopressin (9 aa) , oxytocin (9 aa) , hormones of hypothalamus .
Amino acid derivatives	Catecholamines(derived from the aa Tyrosine which is derived from dietary sources as well as synthesis from Phe) , thyroid hormones
FAs derivatives	Eicosanoids
Steroid hormones	Estradiol , Progesterone , Testosterone , Cortisol , Aldosterone

★ Class'n of hormones based on solubility in aqueous medium in cells :

Hydrophilic(Lipophobic)	Hydrophobic(Lipophilic)
<ul style="list-style-type: none"> ✓ Soluble in aqueous environment ✓ Can't cross the cell membrane \rightarrow they bind to receptor molecules on the outer surface of target cells \rightarrow initiating reactions w/n the cell that ultimately modifies the functions of the cells ✓ Ex \rightarrow Insulin , Glucagon , Epinephrine , GH ,PRL 	<ul style="list-style-type: none"> ✓ Not soluble in aqueous environment . ✓ Can easily cross the cell membrane \rightarrow they can enter target cells \rightarrow bind to intracellular receptors to carryout their action . ✓ Ex \rightarrow Thyroid hormones , Steroid hormones .

★ Hormones are normally present in blood plasma **at very low concentrations**; In blood, hormone binds to **Specific Plasma Carrier Protein**, forming a complex, which is **then transported** in the plasma to distant target cells.

\rightarrow plasma carrier proteins exist for all classes of endocrine hormones \leftarrow

► **Functions** of hormones carrier proteins :

- (1) For **peptide hormones** ► **prevent their destruction** by protease enzymes .
- (2) For **steroid and thyroid hormones** ► significantly **increase the solubility** of these very hydrophobic compounds in plasma (alpha-globulins or albumins)
- (3) For **amino acids-derived hormones** ► **prevent their filtration** by the kidneys ⇒ greatly **prolonging their circulating t(1/2)**

Some properties of Hydrophilic hormones and their receptors

- (1) Receptors are large, integral or transmembrane proteins w/ specificity and high affinity for a given hormone .
- (2) **Reversible binding** b/w the hormone and its receptor .
- (3) Action of hormone depends on **plasma level of hormone**.
- (4) Hydrophilic hormones initiate a response **w/o entering target cells** .
- (5) Hydrophilic hormones causes a **more rapid response** and have a **shorter duration of action** than lipophilic hormones.
- (6) Action of hydrophilic hormones can **last seconds to hours**

The mechanism of action of Lipophilic hormones w/ receptors in target cells

Lipophilic hormone crosses cell membranes to bind w/ Intracellular Receptor ► forming **Hormone-Receptor Complex** ► bind to specific sequence of nucleotide bases in DNA called **HRE** ► binding of Hormone-Receptor Complex to HRE results in ► synthesis of **messenger-RNA** required for **biosynthesis of specific protein**

- ★ Lipophilic hormones are **slower to act** and have **longer duration of action** than Hydrophilic hormones
- ★ Duration of action may range from **hours to days**

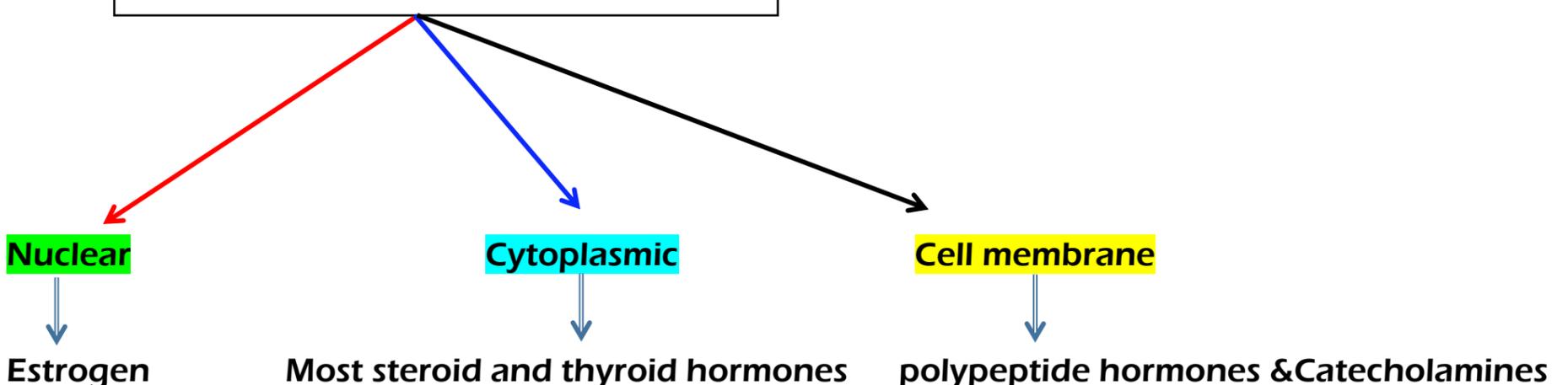
★ **Factors controlling hormone secretions :**

- Stimulatory and Inhibitory agents ► NTs / hypothalamic peptides .
- GnHR ► released in a pulsatile fashion .
- Hormones exhibit **circadian rhythm** ► ACTH , cortisol, PRL , TSH , GH , PTH
- Stress ► inc synthesis and release of hormones .
- Negative feedback control .
- Changes in metabolic products caused by hormone action may exert feedback control .
- Other hormones or drugs may modulate normal endocrine responses.

Blood cortisol

▫ In most ppl , cortisol levels are highest in the morning when they wakeup and lowest around midnight. The body also pumps out excess cortisol when the person is anxious or under intense stress .

Hormone Receptors



- ✓ Hormones are inactivated mainly in ► **Liver** .
- ✓ Inactive metabolites of hormones are excreted mainly in ► **Urine** .
- ✓ T(1/2) for vast majority of hormones is ► **several min - 20 min**
- ✓ T(1/2) for steroid hormones ► **1 h** .
- ✓ T(1/2) for thyroid hormones ► **1 week** .

✓ The final effects of hormone actions :

1. Change the permeability of cell membrane, accelerate the penetration of substrates, enzymes, coenzymes into the cell and out of cell.
2. Acting on the allosteric centers affect the activity of enzymes (**Hormones penetrating membranes**).
3. Affect the activity of enzymes **through the messengers** (cAMP). (**Hormones that can not penetrate the membrane**).
4. Act on the **genetic apparatus of the cell** (nucleus, DNA) and promote the synthesis of enzymes (**Steroid and thyroid hormones**).

Remember the following about hormone receptors :

✓ Structure ⇒ Globular proteins acting as a cell's 'letter boxes' .

✓ Location ⇒ Mostly on the cell membrane .

✓ General principle of action ⇒ Receive messages from chemical messengers coming from other cells ⇒ transmit a message into the cell leading to a cellular effect .

✓ **Different receptors specific for different chemical messengers**

✓ Each cell has a range of receptors in the cell membrane making it **responsive to different chemical messengers**

★ Activation :

Receptors contain a binding site (hollow or cleft in the receptor surface) that is recognised by the chemical messenger ⇒ binding of the messenger involves intermolecular bonds ⇒ results in an induced fit of the receptor protein ⇒ change in receptor shape results in a 'domino' effect ⇒ domino effect is known as Signal Transduction, leading to a chemical signal being received inside the cell

✓ **Binding interactions must be:** (Implies a fine balance)

- **strong enough** to hold the messenger sufficiently long for signal transduction to take place

- **weak enough** to allow the messenger to depart

Chemical messenger does not enter the cell. It departs the receptor unchanged and is not permanently bound